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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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CLARK & ELBING LLP 101 FEDERAL STREET BOSTON, MA 02110			EXAMINER KOSAR, AARON J	
			ART UNIT 1651	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary

Application No.

09/496,231

Applicant(s)

HUBBELL ET AL.

Examiner

AARON J. KOSAR

Art Unit

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Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 January 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 and 51-56 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-19, 51-53, 55 and 56 is/are rejected.
- 7) ☒ Claim(s) 54 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/C)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- Paper No(s)/Mail Date _____

Response to Arguments

Applicant's amendment and argument filed January 15, 2008 in response to the non-final rejection, are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Applicant has amended the claims by amending claims 1, 5, 8, and 13 and introducing new claims 51-56. Claims 1-19 and 51-56 are pending and have been examined on the merits.

DETAILED ACTION

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7 and 11-16, and 18 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-36 of U.S. Patent No. No. 7,291,673 (herein referred to as '**673**'). Although the conflicting claims are not identical, they are not patentably distinct from each other because: both '673 and the instant Application disclose/claim,

for example, a method using: PEG, including PEG diacrylate and/or PEG dithiol compounds, PEG-tetraacrylate, hormones, growth factor (e.g. '673, claims 9, 23, 28, 29, 30, and 31); reaction by (nucleophilic) conjugate addition reaction (e.g. '673, claim 1); reaction of thiol/amine/nucleophile with the two or more conjugated unsaturated groups (e.g. '673, claim 1); and providing a biomaterial therefrom (e.g. '673, claim 1, preamble).

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Applicant has argued that the claims canceled during prosecution of '673 have rendered moot the previous provisional rejection on the ground of nonstatutory obvious-type double patenting over 10/297,229. Respectfully, this is not found to be persuasive since claims 51-52 of '229 were not canceled and correspond to '673 issued claims 1 and 2. Additionally, the instant claims are mired in functional language with respect to describing the method steps and the compositions used by and produced therein. Thus, absent objective evidence to the contrary, '673 embraces and is obvious over the claimed compositions and method steps of the instant claims. Please note, the issuance of '673 subsequent to the previously presented provisional rejection of the instant claims, necessitated the above *non-provisional* obvious-type double patenting rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-19, 51-53, 55 and 56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term “functionalized” is unclear. Whereas components having functionalized moieties (eg. “functionalized components”) possess particular properties and structural features which clearly distinguish the functionalized components, a *method* “wherein components *are* functionalized to comprise..” claims components which are initially un-/minimally-functionalized and then subsequently functionalized through an unclear active step defined as “modifying” (specification, page 11). A method invoking a component and an undefined/unclear method step (functionalizing) merely contemplates the desired product but does not clearly define the modifying step(s)/reaction(s) or the path effecting and correlating the initial components with the desired product(s). It is unclear how one would determine which compounds are capable of functionalizing and by which method(s) to achieve the desired product component. Thus the metes and bounds are unclear.

Applicant has argued that functionalized as exemplified for example by nucleophilic compounds, etc. in the native state versus the respective compounds in need of being functionalized to include such (nucleophilic, etc.) moieties. Applicant has also argued that examples of functionalizing PEG are disclosed.

Applicant’s arguments have been fully considered, however, they are not found to be persuasive, because Applicant’s arguments are directed to limitations not required by the instant claims. The arguments are not persuasive, because the limitation of functionalization - while

argued by Applicant to provide, a nucleophile, etc. to a compound in need thereof *or* to derivatize PEG with a nucleophilic moiety, etc. – are not required by the instant claims.

The functional term “sensitive biological molecule”, defined as “a molecule that is found in a cell, or in a body” (specification, page 12), is indefinite. It is unclear what molecule(s) are necessarily “found” in cells (*eg.* Isotopically enriched dioxygen may be found in cells, etc. but is not naturally present/abundant in cells.); what determines sensitivity; and how sensitive is resolved from insensitive. Thus one would not be apprised as to what compounds the phrase “sensitive biological molecules” embraces and the metes and bounds of the claims cannot be determined.

Applicant has argued that the term is defined as cited on page 12 and that one would be apprised as to the presence of sensitive molecules; however, respectfully, Applicant’s arguments are not found to be persuasive, because the term “sensitive biological molecule” is defined to the extent of “a molecule that is found in a cell, or in a body”. For the reasons of record, the term encompasses an indeterminate number of diatomic or larger molecules known and unknown, of endogenous or exogenous origin, whose common core structure or correlated function is also not recited, and which have an unknown degree of an undisclosed mode of sensitivity to a myriad of undisclosed sensitizing agents for which an undisclosed/unknown sensitized effect results.

Applicant fails to set forth the criteria that define the alleged critical features at the point of novelty of the invention other than providing functional definitions as made of record and as argued above. Such functional language describes nothing about the chemical, physical, or

structural properties of these compounds. Attention is directed to *General Electric Company v. Wabash Appliance Corporation* 37 USPQ 466 (US 1938), at 469, speaking to functional language at the point of novelty as herein employed.: “the vice of a functional claim exists not only when a claim is ‘wholly’ functional, if that is ever true, but when the inventor is painstaking when he recites what has already been seen, and then uses conveniently functional language at the exact point of novelty”. Functional language at the point of novelty is further admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC 1997) at 1406: stating this usage does “little more than outline goals appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate”. Claims employing functional language at the point of novelty neither provide those element required to practice the invention, nor “inform the public during the life of the patent of the limits of the monopoly asserted.”, *General Electric Co. v. Wabash Appliance Corp.*, at 468.

Please note, arguments attempting to substantiate the claimed process, insofar as these processes rely on the use of components which instead of being characterized by technical features suitable for the identification of the components, is imprecisely defined by means of functional features which merely recite the desired result to be achieved; and, further, the subject matter may still be considered to be obvious by the disclosure of prior art/other processes and components, though not defined by said functional language of the instant claims. Thus, for the reasons above, the claims are maintained as rendered indefinite.

Claim Objections

Claim 54 is objected to as being dependent upon a rejected base claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-19 and 51-53 are rejected under 35 U.S.C. 103(a) as being obvious over HUBBELL (Hubbell, J.A., “Hydrogel Systems for Barriers and Local Drug Delivery in the Control of Wound Healing” J. Controlled Release. 1996, 39, 305-313.) as evidenced by HARATA (Harata, K., Abe, Y., and Muraki, M. Full-matrix Least Squares Refinement of Lysozymes and Analysis of Anisotropic Thermal Motion” Proteins. 1998, 30, pages 232-243 and Harata, K., et al. “PDB: 1JSF” GenomeNet:DBGet <http://www.genome.jp/dbget-bin/www_bget?pdb+1JSF> archived 1/05/1998 (accessed online 5/16/2008), 5 pages.) and in view of MARCH (March, J., “Addition to Carbon-Carbon Multiple Bonds” Advanced Organic Chemistry: Reactions, Mechanisms, and Structure. 4th Ed., 1992. Chapter 15, pages 734-770 and 795-797).

HUBBELL teaches an *in vivo* biodegradable, hydrogel-forming ABA-copolymer comprising PEG diacrylate (“ α,ω -diacrylated PEG”, PEGDA: page 307, section 2.1, ¶1 and page 308, ¶1, last sentence.). Hubbell also teaches combining a PEGDA (the PLA-linked PEGDA derivative) with, for example, lysozyme and forming a hydrogel therefrom. Hubbell also teaches that the hydrogel may be synthesized by combining with an accelerator, by teaching each of polymerization initiator, cocatalyst, or a Xe arc lamp exposure (page 308, ¶2-3).

As evidenced by HARATA, lysozyme (PDB entry: 1JSF) comprises the 130 amino acid sequence as follows (emphasis added):

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LYS VAL PHE GLU ARG CYS GLU LEU ALA ARG THR LEU LYS
 ARG LEU GLY MET ASP GLY TYR ARG GLY ILE SER LEU ALA
ASN TRP MET CYS LEU ALA LYS TRP GLU SER GLY TYR ASN
 THR ARG ALA THR ASN TYR ASN ALA GLY ASP ARG SER THR
 ASP TYR GLY ILE PHE GLN ILE ASN SER ARG TYR TRP CYS
 ASN ASP GLY LYS THR PRO GLY ALA VAL ASN ALA CYS HIS
 LEU SER CYS SER ALA LEU LEU GLN ASP ASN ILE ALA ASP
 ALA VAL ALA CYS ALA LYS ARG VAL VAL ARG ASP PRO GLN
 GLY ILE ARG ALA TRP VAL ALA TRP ARG ASN ARG CYS GLN
ASN ARG ASP VAL ARG GLN TYR VAL GLN GLY CYS GLY VAL

which intrinsically comprises several strong nucleophilic groups (e.g. the underlined residues above comprise -SH / -S-S- (Cys); -OH (Ser, Thr, and Tyr); and -NH₂ (Asn, Gln, Arg, and N-terminal Lys) not involved in the peptide backbone linkages (HARATA, SEQRES).

MARCH teaches that addition reactions to C-C multiple bonds are known. March teaches reaction between carbon-carbon double bonds and compositions having sulfur-containing moieties (§5-6) and nitrogen-containing moieties (§5-7), including nucleophilic addition (pages 741-743) reactions; including free-radical reactions (pages 743-745); and additions to conjugated systems or Michael additions (pages 745-747 and 795-797, respectively) (that compositions having an RSH moiety (H₂S or thiols wherein R may "contain various functional groups") react with olefins or double bonds by free-radical mechanism in the presence of free-radical initiators, but also add by electrophilic or nucleophilic mechanisms, wherein the compositions may include Michael type substrates (i.e. RS group addition to C=C-C=O system)(e.g. March, pages 766-767, including footnote 197).

Hubbell differs from the instant claims in that whereas Hubbell teaches polymerization to form a gel, including components having the instantly claimed moieties, and the use of accelerators, Hubbell teaches photopolymerization but is silent regarding an underlying or

alternative nucleophilic reaction directly between the lysozyme nucleophilic moieties and the PEGDA terminal vinyl groups.

It would have been obvious to react the hydrogel-forming composition of Hubbell by a method other than or in addition to photopolymerization and with combinations other than divinyllic (free-radical) reactions because Hubbell teaches a method of polymerizing a composition containing acrylate groups (a C=C containing moiety) in the presence of a SH, NH, and OH, and because MARCH teaches that reaction between compounds having vinyl groups and compounds having SH groups are known. March also beneficially teaches that free-radical reactions and nucleophilic reactions are known for the same purpose of adding compounds having SH (or NH) groups to compounds with unsaturated/conjugated/etc bonds. Though Hubbell is directed towards a dominant or competitively favorable vinyl-vinyl linkage, the presence of precursor compounds therein having SH, NH, etc. groups (e.g. lysozyme) in the reaction would intrinsically form a degree of linkages between lysozyme moieties and the PEG acrylate especially in the absence of objective evidence to the contrary or criticality of a particular undisclosed reaction/property. Thus, one recognizing the presence of nucleophiles and C=C (and conjugated acrylate) moieties in the addition/polymerization reactions of Hubbell, in view of the teachings of March, would be motivated to substitute nucleophilic-promoting conditions for free-radical promoting condition to obtain the desired product. Furthermore, one would have had a reasonable expectation of success in making a PEG diacrylate:lysozyme polymerized composition, because the success depends upon the reaction of known substrates, taught by the prior art to have known functional groups which react in a known and predictable

manner and especially in the absence of objective evidence to the contrary of evidence to the criticality of some undisclosed property.

To the extent that Hubbell may differ from the instantly claimed invention, regarding a particular PEG MW, it would have been obvious to use any compound having a PEG because said compounds share a common chemical PEG core and because Hubbell teaches that various PEG compositions may be used for the same purpose/utility, i.e. having hydrogel/tunable controlled-release properties which may be effected, teaching "by adjusting the molecular mass of the PEG, either lower (PEGs as low as 200 Da form good gels) or higher (PEGs at least up to 35,000 Da form good gels)"(c.g page 311, §3.3). The MPEP states, "A prima facie case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). See *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and *In re Dillon*, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991)." See MPEP § 2144.09.

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12

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USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

KUDELA(Kudela, V. "Hydrogels" Encyclopedia of Polymer Science and Engineering, 1987, (Ed. Mark, H., et al.), vol.7, pages 783-807.) *teaches general hydrogel-forming compositions classes and the use of polyfunctional precursors. Kudela also teaches that "hydrogels are usually formed by copolymerization and cross-linking" and that hydrogel-forming derivatives of hydroxyethyl esters of acrylic acid and methacrylic acid are the most important (e.g. page 797, ¶1-3).*

Applicant's amendment necessitated new ground(s) of rejection presented in this Office action; however, because additional new grounds of rejection are presented herein, **THIS ACTION IS MADE NON-FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

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will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aaron J. Kosar whose telephone number is (571) 270-3054. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Aaron Kosar
Examiner
Art Unit 1651

/Sandra Saucier/
Primary Examiner, Art Unit 1651